

**REMARKS/ARGUMENTS**

Claims 1-17 were pending in the above-captioned application. Claims 8, 9 and 13-17 were withdrawn from consideration. Claim 1 has been amended to more particularly point out and distinctly claim that which Applicants consider to be their invention.

Upon entry of the above-made amendments, therefore, claims 1-17 will be pending in the current application. The amended claims are fully supported in the specification as originally filed (page 4, line 10 of the specification). The amendments to the Claims do not add new matter. Applicants respectively request that the amendments be entered.

The following remarks, in conjunction with the above amendments, are believed to be fully responsive to the Office Action.

**THE REJECTION UNDER 35 U.S.C. § 102 SHOULD BE WITHDRAWN**

Claim 1 is rejected under 35 U.S.C. 102(b) as being anticipated by Vaughn U.S. Patent 5,242,392 ("Vaughn"). In response, Applicants submit that the rejection should be withdrawn for the reasons stated below.

As noted above, claim 1 has been amended to recite "to enhance product homogeneity".

A finding of anticipation under 35 U.S.C. 102 requires the disclosure in a single prior art reference of each element of the claim under consideration. *W.L. Gore & Associates v. Garlock, Inc.*, 721 F.2d 1540, 220 USPQ 303 (Fed. Cir. 1983). There must be no difference between the claimed invention and the reference disclosure, as viewed by a person of ordinary skill in the field of the invention. *Scripps Clinic & Research Found. v. Genetech Inc.*, 927 F.2d 1565, 18 USPQ 2d 1001, 1010 (Fed. Cir. 1991).

The present invention is drawn to administration of a gravity segregating dispersion, such as a gas-containing contrast agent, by continuous infusion. The dispersion is delivered from an upper or lower extremity of an essentially vertically positioned delivery vessel, and is admixed with a flushing medium prior to administration to a subject. The present invention has identified a solution to the problem of administering a gravity segregating dispersion, such as microbubbles that tend to float. By combining delivering from the top or bottom of a vertically positioned vessel and admixing with a flush medium prior to administration to a patient, the segregation is minimized and enhanced product homogeneity is achieved.

Vaughn discloses an intravenous piggyback flush apparatus for administration of medicaments into a patient by force of gravity. Vaughn does not however describe administration wherein a gravity segregating dispersion is admixed with a flushing medium prior to administration to the patient. Vaughn describes an apparatus and method that reduces the number of needle sticks required during the course of treatment. This is done by including a flush chamber in the apparatus that is connected to the conventional IV tubing. It is specifically stated that the flush chamber is positioned lower than the IV bag (medicament), so that the contents of the IV bag empty before the contents of the flush chamber empty (col. 4, lines 55-57 and col. 5-12). Any residual medicaments that remain in the tube after administration from the IV bag, will be flushed into the patient by the flushing medium. Hence, Vaughn administers the medicaments and then flush with a flushing medium. In the present invention the "medicament" (segregating dispersion) is mixed with a

flushing medium prior to administration to the patient to get a maximum mixing and a homogeneous suspension prior to administration. Vaughn fails to teach all steps of the instant claim 1, and actually teaches away from the instant invention specifically stating that the medicament is administered before the flushing media. The instant claim is therefore believed to be novel over Vaughn.

Thus, Applicants respectfully submit that the Examiner's rejection under 35 U.S.C. 102 (b) has been overcome and/or obviated and respectfully request that the rejections be withdrawn.

**THE REJECTION UNDER 35 U.S.C. § 103(a) SHOULD BE WITHDRAWN**

Claims 1-3 are rejected under 35 U.S.C. 103(a) as being obvious over Vaughn in view of Remington, The Science and Practice of Pharmacy 19<sup>th</sup> edition, pages 1552-1554 ("Remington"). Further, claims 1-7, 10-12 are rejected under 35 U.S.C. 103(a) as being obvious over Vaughn in view of Remington and further in view of Unger, WO 97/48337 ("Unger"). In response, Applicants submit that each of these rejections should be withdrawn for the reasons stated below.

Remington describes various ways of administering a medicament. These are (page 1552, second paragraph): Direct intravenous injection, Volume control method and Piggyback method. The piggyback method is the only method described that has flushing medium in a separate container. For this method it is described that the medicament is entered "on top" of a primary IV fluid to e.g. reduce irritation (page 1553, second paragraph). Remington describes a method switching between administration of a drug solution and an intravenous fluid, and to achieve this, one container is hung lower than the other container. Hence, Remington does not describe admixture of a medicament with a flushing medium prior to administration to a subject and actually teaches away from this specifically stating that one container is emptied before the other.

Remington does describe that infusion pumps may be used, but such are described as a separate technique and not in combination with use of a flushing medium. As Remington specifically states that infusion pumps do not depend on gravity to provide the pressure required (page 1554, second col.) there is clearly no indication that if using a syringe placed in a syringe pump it should be placed in a vertical position. A combination of Vaughn and Remington does not indicate the aspect of admixing a dispersion with a flushing medium prior to administration.

Unger is drawn to ultrasound contrast agents and delivery of such to a patient. However, also Unger fails to teach admixing of the contrast agent with a flushing agent. On page 70, first paragraph, Unger describes methods using flushing, stating "To promote the transport of the lipid and/or vesicle composition from the injection site into the bloodstream and, thereafter, to the region of interest, a flush may be administered. The flush may act, generally by mechanical action, to "push" or "wash" the injected composition into the bloodstream. Thus in embodiments which may involve, for example, diagnostic ultrasound of myocardial tissue with a contrast agent that comprises a lipid and/or vesicle composition, a flush may be administered **after** injection of the lipid and/or vesicle composition to facilitate its movement through the circulatory system and delivery to the region of interest, for example, the heart region". See also page 71, second paragraph and page 74, second paragraph for further illustrations of that any flushing media is administered after the contrast agent. Hence, Unger does not teach admixing. Unger indicates in figure 2 that the contrast agent can be administered from a vertically positioned syringe, but there is no teaching in the specification that the syringe is placed in this position to avoid segregation. If using a three-way connector as indicated in Figure 2 to connect the flushing media and the contrast agent syringe, it would for practical reasons be easiest to place one delivery vessel horizontally and one vertically. As Unger has not described why the syringe with the contrast agents has been positioned vertically it seems incidental that it is the vessel with the contrast agent that has been placed in this position and not the vessel with the infusion media. As argued above claim 1, and subsequent claims, are not obvious based on the references, as none of these suggest admixing of a segregating dispersion with a flushing media prior to administration to enhance product homogeneity.

Thus, Applicants respectfully request that the rejections be withdrawn.

### **CONCLUSIONS**

In view of the amendments and remarks herein, Applicants believe that each ground for rejection or objection made in the instant application has been successfully overcome or obviated, and that all the pending claims are in condition for allowance. Withdrawal of the Examiner's rejections and objections, and allowance of the current application are respectfully requested.

The Examiner is invited to telephone the undersigned in order to resolve any issues that might arise and to promote the efficient examination of the current application.

Respectfully submitted,



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